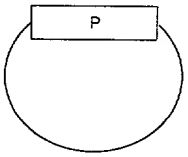
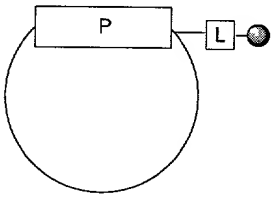
EXHIBIT A - PENDING CLAIMS
THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A method of synthesis of a cyclic peptide or peptidomimetic compound of General Formula I



General Formula I

or General Formula II



General Formula II

where L is a linker unit, linking the cyclic peptide to a

solid support  in which the cycle is a monocycle,
bicycle or higher order cycle comprising 1 to 15 monomers, comprising the steps of:

a) inducing flexibility in the peptide or peptidomimetic compound by reversible *N*-substitution or by forcing a *cis* amide bond conformation using a *cis*-amide bond surrogate to facilitate cyclisation, and, if necessary,

b) subjecting the cyclic peptide or peptidomimetic compound to a ring contraction reaction.

2. A method according to claim 1, in which the cycle comprises 1 to 10 monomers.

3. A method according to claim 2, in which the cycle comprises 1 to 5 monomers.

4. (Amended) A method according to claim 1, in which the cycle is a monocycle.

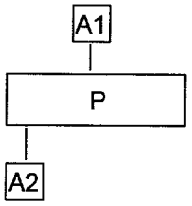
5. (Amended) A method according claim 1, in which the cycle is a bicycle.

6. (Amended) A method according to claim 1, in which the cycle comprises more than two rings.

7. (Amended) A method according to claim 1, in which the compound is of General Formula II, and the linker L is attached to a backbone nitrogen or to an atom in the side chain of the monomer.

8. (Amended) A method according to claim 1, which is carried out in solution, comprising the steps of:

a) Preparing a linear peptide of General Formula III



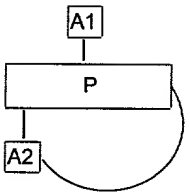
General Formula III

where P is a linear peptide of 1 to 15 monomers;

A1 is one or more N-substituents, either reversible or non-reversible, on the peptide backbone, or is a chemical moiety that forces a *cis* conformation of the backbone, and

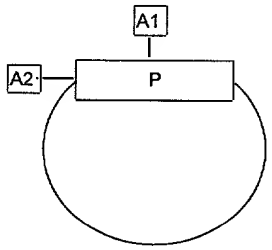
A2 is a covalently-bonded group of atoms comprising a reactive functionality to form an initial large cyclic peptide prior to ring contraction to the desired substituted cyclic peptide;

b) Activating the *C*-terminus to form a cyclic peptide of General Formula IV:



General Formula IV

c) Permitting the peptide of General Formula IV to rearrange via a ring contraction reaction (which may occur spontaneously) to form a cyclic peptide of General Formula V; and optionally



General Formula V

d) Subjecting the cyclic peptide of General Formula V to a deprotection reaction to remove the groups A1 and A2 to yield the desired cyclic peptide of General Formula I.

9. A method according to claim 8, in which P is a linear peptide of 1 to 10 monomers.

10. A method according to claim 9, in which P is a linear peptide of 1 to 5 monomers.

11. (Amended) A method according to claim 8, in which A1 and/or A2 is left attached to the peptide.

12. A method according to claim 11, in which A1 and/or A2 is subsequently linked to a solid support, derivatised, or linked to another cyclic peptide or peptidomimetic compound.

13. (Amended) A method according to claim 8, in which A1 is a reversible N-substituent.

14. A method according to claim 13, in which A1 is a 2-hydroxy-4-methoxybenzyl, 2-hydroxybenzyl or 2-hydroxy-6-nitrobenzyl substituent.

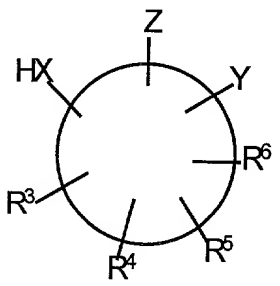
15. (Amended) A method according to claim 8, in which A2 is eliminated by spontaneous ring contraction.

16. (Amended) A method according to claim 8, in which A2 comprises a nucleophile that reacts rapidly with a *C*-terminus to form an initial large ring, which then contracts either spontaneously, or upon heating or additional chemical treatment.

17. A method according to claim 16, in which A2 is thiol or hydroxyl.

18. (Amended) A method according to claim 8, in which A2 is an irreversible substituent, is removed after ring contraction, or is eliminated spontaneously upon ring contraction.

19. (Amended) A method according to claim 8, in which A2 is a compound of general formula (a):



(a)

in which the ring

(a) optionally comprises one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulphur;

(b) is of 5 to 7 atoms;

(c) comprises 3 carbon atoms substituted respectively by XH, Z, and Y; and

(d) is additionally substituted by groups R^3 and R^4 when the compound is a 5-membered ring, or is additionally substituted by groups R^3, R^4, and R^5 when the

compound is a 6-membered ring, or is additionally substituted by groups R3, R4, R5 and R6 when the compound is a 7-membered ring,

in which

X is oxygen, sulphur, CH_2O-, or CH_2S-;

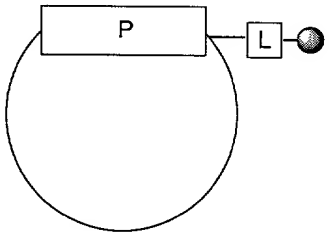
Y is an electron-withdrawing group;

Z is any group which allows the formation of a covalent carbon-nitrogen bond; and

R^3, R^4 and R^5 are each independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroaryl, substituted heteroaryl, alkoxy, aryloxy, XH or Y, or a covalent linkage to a solid support, and

in which R^3 and R^4 or R^4 and R^5 can optionally together with the ring form a 5-, 6-, or 7- membered ring.

20. A method of solid-phase synthesis of a cyclic peptide or peptidomimetic compound of the structure:

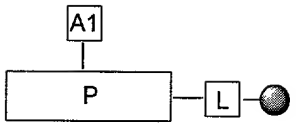


General Formula II

where L is a linker unit, linking the cyclic peptide to a

solid support ●, comprising the steps of:

a) synthesis of a linear peptide of General Formula VI, bound to a solid support via a linker L,



General Formula VI

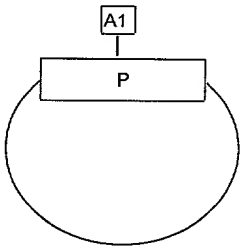
in which P is a linear peptide of 1 to 15 monomers, and

A1 is one or more N-substituents either reversible or non-reversible, on the peptide backbone, or is a chemical moiety that forces a *cis* conformation of the backbone, and

L is a linker between any atom of the peptide and the solid support, and

(b) either

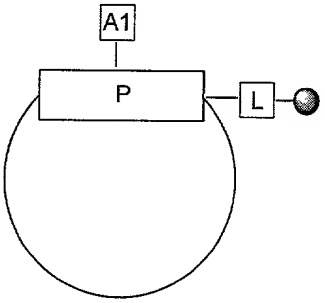
(i) subjecting the peptide to cyclisation and concomitant cleavage from the solid support to yield a cyclic peptide of General Formula VII,



General Formula VII

followed by selective removal or derivatisation of A1, if necessary followed by side chain deprotection of the peptide and removal of A1 to yield the desired cyclic peptide of General Formula I; or

(ii) cyclisation of the peptide to yield a second solid support bound cyclic peptide of General Formula VIII,



General Formula VIII

and subjecting the compound of General Formula VIII to removal of A1 and of any peptide side chain protecting groups, and cleavage from the solid support to yield the desired cyclic peptide of General Formula I.

21. (Amended) A method according to claim 20, in which the linker L is attached to a backbone nitrogen or an atom in the side chain of the monomer.

22. (Amended) A method according to claim 20, in which the cycle is a monocycle.

23. (Amended) A method according to claim 20, in which the cycle is a bicycle.

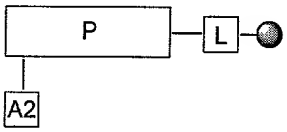
24. (Amended) A method according to claim 20, in which the cycle comprises more than two rings.

25. (Amended) A method according to claim 20, in which side chain deprotection of the peptide, removal of A1 and cleavage from the solid support are performed separately.

26. (Amended) A method according to claim 20, in which side chain deprotection of the peptide, removal of A1 and cleavage from the resin are performed concurrently.

27. A method of solid-phase synthesis of a cyclic peptide, comprising the steps of:

a) preparing a linear resin-bound peptide of General Formula IX:



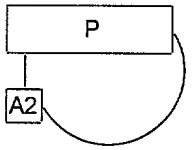
General Formula IX

where P is a linear peptide of 1 to 15 monomers;

A2 is a covalently-bonded group of atoms comprising a reactive functionality to form an initial large cyclic peptide prior to ring contraction to the desired substituted cyclic peptide;

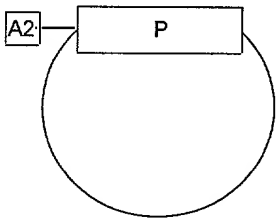
L is a linker between any atom of the peptide and the solid support, and

b) subjecting the peptide of General Formula IX to cyclisation and concomitant cleavage from the resin to yield a cyclic peptide of General Formula I;



General Formula X

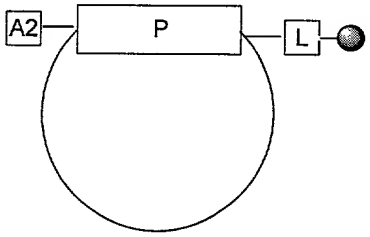
c) allowing the cyclic peptide X to undergo ring contraction (which may occur spontaneously) to yield a second cyclic peptide of General Formula XI, and



General Formula XI

d) either derivatising the group A2, or removing A2 to yield the desired cyclic peptide of General Formula I.

28. A method according to claim 27, in which the linear resin-bound peptide of General Formula IX is subjected to initial cyclisation and ring contraction on the solid support to yield a solid support-bound cyclic peptide of General Formula XII,



General Formula XII

and either

(i) cleaved from the solid support to yield an A2- substituted cyclic peptide, or

(ii) deprotected and cleaved from the solid support to yield a cyclic peptide of General Formula I.

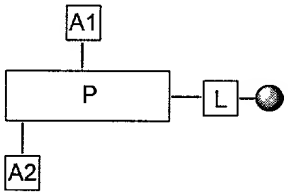
29. A method according to claim 28, in which A2 is derivatised in solid phase or in solution.

30. (Amended) A method according to claim 28, in which side chain deprotection of the peptide, removal of A1 and cleavage from the resin are performed separately.

31. (Amended) A method according to claim 28, in which side chain deprotection of the peptide, removal of A1 and cleavage from the solid support are performed concurrently.

32. A method of solid phase synthesis of a cyclic peptide, comprising the steps of

a) synthesis of a linear solid support-bound peptide of General Formula XIII,



General Formula XIII

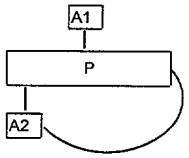
where P is a linear peptide of 1 to 15 monomers;

A1 is one or more N-substituents, either reversible or non-reversible, on the peptide backbone, or is a chemical moiety that forces a *cis* conformation of the backbone, and

A2 is a covalently-bonded group of atoms comprising a reactive functionality to form an initial large cyclic peptide prior to ring contraction to the desired substituted cyclic peptide;

L is a linker between any atom of the peptide and the solid support, and

b) subjecting the peptide of General Formula XIII to cyclisation and concomitant cleavage from the solid support to yield a cyclic peptide of General Formula XIV,



General Formula XIV

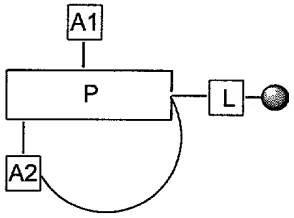
c) subjecting the cyclic peptide of General Formula XIV to ring contraction (which may be spontaneous), and

d) cleaving the groups A1 and A2 to yield the desired cyclic peptide of General Formula I.

33. A method of solid phase synthesis of a cyclic peptide, comprising the steps of;

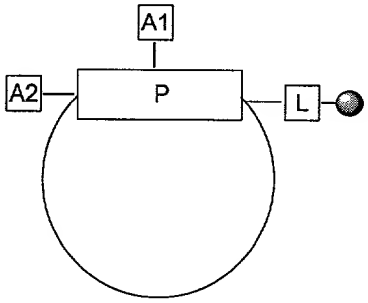
a) synthesis of a linear solid support-bound peptide of General Formula XIII,

b) subjecting the linear peptide to cyclisation on the solid support to yield a cyclic peptide of General Formula XV,



General Formula XV

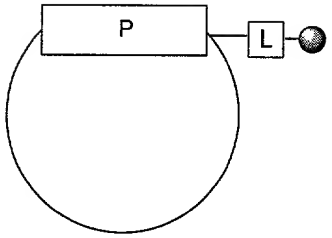
c) subjecting the cyclic peptide to ring contraction (which may occur spontaneously) to yield a cyclic peptide of General Formula XVI,



General Formula XVI

and either

d) cleaving groups A1 and A2 while the peptide is bound to the solid support to yield a resin-bound cyclic peptide of General Formula II, or



General Formula II

e) subjecting the cyclic peptide to deprotection and concomitant cleavage from the solid support to yield the desired cyclic peptide of General Formula I.

34. A method according to claim 33, in which side chain deprotection of the peptide, removal of A1 and cleavage from the solid support are performed separately.

35. A method according to claim 33, in which side chain deprotection of the peptide, removal of A1 and cleavage from the solid support are performed concurrently.

36. (Amended) A method according to claim 1, in which one or more of the monomers carries a side chain protecting group.

37. (New) A method according to claim 20, in which one or more of the monomers carries a side chain protecting group.

38. (New) A method according to claim 27, in which one or more of the monomers carries a side chain protecting group.

39. (New) A method according to claim 32, in which one or more of the monomers carries a side chain protecting group.

40. (New) A method according to claim 33, in which one or more of the monomers carries a side chain protecting group.

41. (New) cyclo [Tyr-Arg-D-Phe Gly].

42. (New) cyclo [Tyr-Arg-Phe-Gly].

43. (New) A composition comprising a cyclo [Tyr-Arg-D-Phe Gly] and/or cyclo [Tyr-Arg-Phe-Gly], together with a pharmaceutically acceptable carrier.